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Alveolar Soft Part Sarcoma Metastatic to the Breast

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Metastasis to the breast is uncommon, with an incidence of 0.5–3%. Alveolar soft part sarcoma is rare, accounting for <1% of malignant soft tissue tumors, which are themselves unusual. Excluding contralateral breast and hematologic malignant disease, the primary lesion in most cases of metastasis to the breast is melanoma, small cell carcinoma of the lung, or ovarian carcinoma, although rhabdomyosarcoma is the most common primary tumor in children. We describe a 26-year-old woman with no history of malignant disease who presented with two masses in the right breast that clinical evaluations and ultrasonography indicated were fibroadenomas. Pathological studies after excisional biopsy, however, indicated alveolar soft part sarcoma. Subsequent computed tomography showed the primary tumor in the anterior left thigh and multiple bilateral lung metastases. Because of the presence of distant metastases, the patient was treated with chemotherapy.

KEY WORDS: **alveolar soft part sarcoma, cancer, breast, metastasis, thigh**

INTRODUCTION

Metastasis to the breast from an extramammary neoplasm is rare; only about 300 cases have been reported [1]. In most adult patients, excluding those with a hematologic malignant disease, the primary lesion is melanoma or carcinoma of the lung or ovary [2–4]. We describe a patient with alveolar soft part sarcoma that metastasized to the breast from a primary tumor in the thigh.

CASE REPORT

A 26-year-old woman presented with two masses in the upper outer quadrant of the right breast that she had first observed a month earlier. The patient had no history of malignant disease and no risk factors for breast cancer. On physical examination, both masses were deep, relatively well demarcated, and movable, indicating fibroadenoma. No axillary lymphadenopathy, nipple discharge or retraction, or skin changes were observed. Because of the patient's age, a mammographic evaluation was not done, but ultrasonography demonstrated well-defined hypoechoic masses with enhanced-through transmission, also suggesting fibroadenoma (Fig. 1). However, an aspiration cytology study of one of the masses showed atypical cells.

The patient underwent excisional biopsy of both breast masses. On gross examination, the masses were similar. They were fairly well delineated from the surrounding adipose tissue and were 1.2 cm and 1.5 cm in diameter, respectively. Both tumors were relatively soft and had a pink-tan, friable, cut surface.

Microscopically, the tumors were composed of large polyhedral cells with abundant eosinophilic granular cytoplasm, large vesicular nuclei, and prominent nucleoli (Fig. 2). The tumor cells grew in both alveolar and solid patterns. Infiltration of the surrounding breast parenchyma and vascular invasion were present at the edge of the tumors (Fig. 3). Immunohistochemical stains showed positive staining for vimentin, S100, and neuron-specific enolase and focal staining for desmin. There was no staining for keratin, epithelial membrane antigen, carcinoembryonic antigen, melanoma-associated antigen HMB-45, leukocyte common antigen, or alpha-fetoprotein. A DNA analysis showed aneuploidy. Electron mi-

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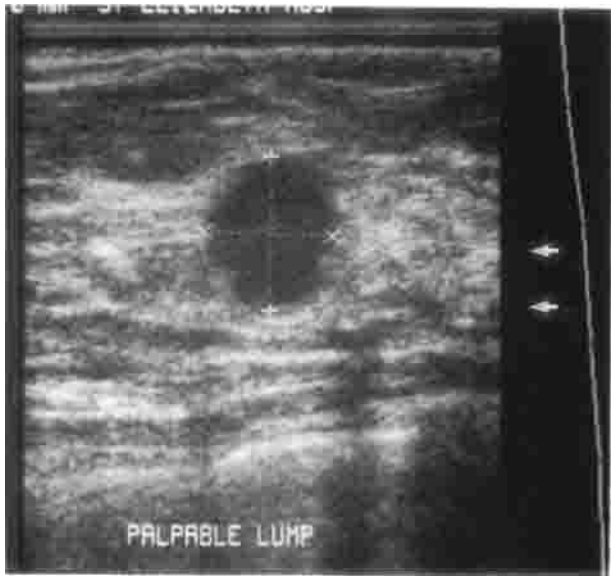

Fig. 1. Ultrasonographic image showing hypoechoic mass with through transmission.

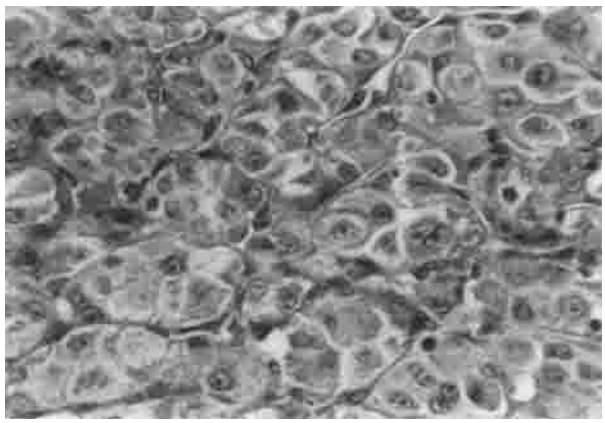

Fig. 2. Light microscopical study showing tumor composed of large polyhedral cells with abundant eosinophilic cytoplasm, prominent nucleoli, and rare mitoses (H & E, ×400).

croscopy demonstrated membrane-bound intracytoplasmic crystals (Fig. 4), diagnostic of alveolar soft part sarcoma.

The patient was reexamined. A physical examination and computed tomography (CT) scan showed a large mass (8 × 4 × 4 cm) in the anterior left thigh. Staging CT scanning of the chest, abdomen, and pelvis revealed multiple bilateral lung metastases but no evidence of adenopathy or metastatic disease in the abdomen or pelvis.

Because of the presence of distant metastases, the patient was not considered to be a candidate for a definitive surgical procedure. She was treated with chemotherapy. Two years after diagnosis, additional multiple metastases to both breasts and both lungs had developed.

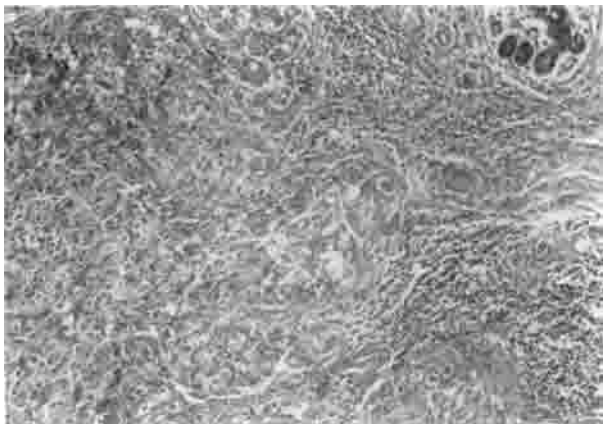

Fig. 3. Light microscopical study showing tumor infiltration of surrounding breast parenchyma (H & E, ×100).

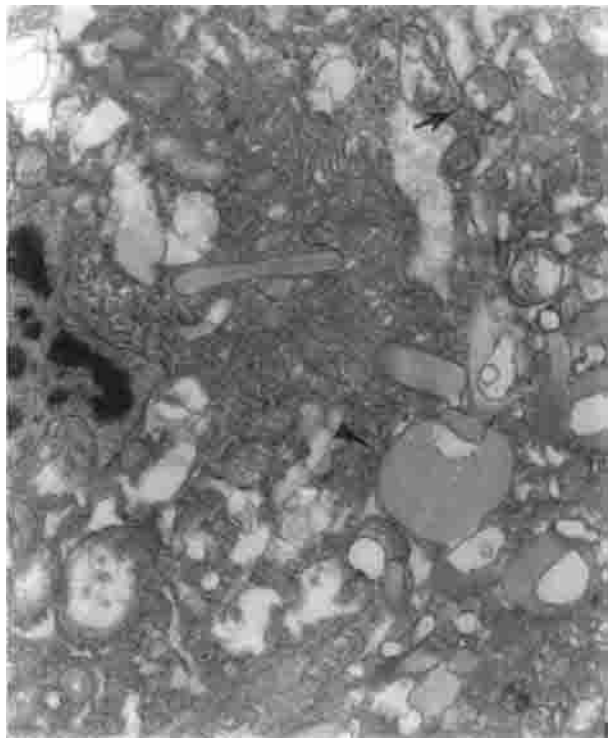

Fig. 4. Electron microscopical study showing neoplastic cells rich in mitochondria (arrow), with some containing membrane-bound crystals (arrowhead) (H & E, ×24,300).

DISCUSSION

The incidence of metastasis to the breast has been estimated to range from 0.5% to 3% [3,5]. Lymphoma and melanoma are the most common extramammary primary lesions associated with such dissemination, followed by lung carcinoma of various histologic types [1]. Carcinoma of the ovary, prostate, and stomach have been found in several patients with breast metastasis [3,6], as

has carcinoid [1]. Rhabdomyosarcoma is the most common primary tumor in children with metastasis to the breast [1,2]. In a 1982 review, Paulus and Libshitz [5] observed that a total of 22 cases of metastasis to the breast from soft tissue sarcomas had been reported in case discussions and autopsy series in the literature and mentioned that one of their patients had alveolar soft part sarcoma metastatic to the breast. However, they provided no details about the case. Subsequently, a few other cases of sarcoma metastatic to the breast were described [1,4], but we could find no other report of a breast metastasis from an alveolar soft part sarcoma.

Only about 2% of cancers are malignant soft tissue tumors, and alveolar soft part sarcoma accounts for approximately 1% of soft tissue sarcomas [7]. The primary lesion is in the lower extremity in about 60% of patients [7], including ours. Alveolar soft part sarcoma is characterized clinically by slow growth, an early high frequency of distant metastases, local recurrence late in the disease course, and fatality. Metastasis occurs in about 68% of cases and most often affects the lungs, brain, and skeleton; dissemination is generally through the hematogenous route [8]. Lymph node metastasis is uncommon. Asymptomatic pulmonary metastasis in a clinically well patient at presentation is characteristic of alveolar soft part sarcoma and occurred in our case. Interestingly, in up to 40% of patients with metastasis to the breast from an extramammary source, the breast lesion is the first manifestation of disease [9,10].

Lieberman et al. [8] found that if metastases were present at diagnosis of alveolar soft part sarcoma, the median survival time was 3 years. Nevertheless, early metastasis did not preclude a long survival time in several of their patients. In general, metastatic disease to the breast implies widespread dissemination and overall poor survival [4]. Among patients with metastatic disease in the breast from all sites, about 80% die in the first year after diagnosis [2,4]. However, prolonged survival may be expected in patients with a malignant disease that has an indolent clinical course, such as carcinoid, or a disorder for which there is effective chemotherapy, such as lymphoma or ovarian carcinoma [2,9]. Our patient with alveolar soft part sarcoma metastatic to the breast is alive 2 years after diagnosis.

Patients with alveolar soft part sarcoma are generally between 20 to 30 years old [7,8,11]; Lieberman et al. [8] found that the tumor is more likely to develop in women than in men. Most patients with metastatic disease to the breast are women between 40 and 50 years old [3]. At 26 years old, our patient was more typical of those with alveolar soft part sarcoma. In addition, she was a member of the age group chiefly affected by breast fibroadenoma, which is what her breast masses appeared to be on ultrasound examination [12].

Alveolar soft part sarcomas are usually circumscribed, nonencapsulated, soft, and friable. They may be difficult to distinguish pathologically from some usually benign lesions, such as paragangliomas [11], or from malignant tumors such as melanoma or renal cell carcinoma [13]. In our patient, the diagnosis was confirmed by immunohistochemical staining and electron microscopy.

Metastasis to the breast is thought to occur mostly by means of hematogenous spread, although lymphatic spread is observed when the primary tumor is in the contralateral breast [5]. Most breast metastases occur in younger women because of the greater vascularity of their breasts as compared with those of older women. The role of hormonal status as a predisposing factor remains controversial [1]. Metastases to the breast generally present as solitary nodules in the upper outer quadrant, which has the most abundant glandular tissue and thus the best blood supply [1,2]. They are painless unless bulky and tend to be round, firm, and movable, simulating fibroadenoma, although their rapid growth indicates malignant disease. In about half the cases, metastases to the breast are superficially located [2]. Skin changes and nipple retraction or discharge do not occur; however, large tumors or those affecting the dermal lymphatics may adhere to the skin [4]. Axillary involvement is present in 25–58% of cases [1].

Pathologically, a metastasis to the breast may be difficult to distinguish from a primary lesion, especially when evaluating a frozen section from a patient with no history of neoplasm [4,14]. The pathological diagnosis depends on the presence of a well-circumscribed but nonencapsulated tumor with atypical histologic features, a periductal or perilobular distribution of malignant cells with an absence of an intraductal component or in situ carcinoma, the presence of normal surrounding breast tissue showing no desmoplastic reaction, and the presence of numerous lymphatic emboli [1,2]. Electron microscopy and immunocytochemical studies may be needed to confirm the diagnosis, as in our case. Excisional biopsy is usually required for pathological confirmation of the diagnosis, and it also provides adequate local control.

On mammography, metastases to the breast are typically round and dense. Microcalcifications are almost never observed, except in rare cases of metastasis from ovarian carcinoma [5]. Because a metastatic breast mass does not cause a desmoplastic response in adjacent normal tissue, it is about the same size on palpation and mammography [14]. In contrast, in primary breast carcinoma, the mass is often smaller on the mammogram. Breast metastases may sometimes have the mammographic appearance of fibroadenomas or cysts [5,6]. In our case, the breast metastases mimicked fibroadenomas on an ultrasound study. Paulus and Libshitz [5] observed that differentiating between a solitary breast metastasis and a primary breast cancer may be difficult radiologically when slow-growing and circumscribed tumors are

involved. They mentioned medullary carcinoma and mucin-producing carcinoma in this context, but this also occurred in our patient with alveolar soft part sarcoma.

Alveolar soft part sarcoma is generally treated with wide excision of the primary lesion. No survival advantage has been demonstrated in patients who have received chemotherapy, radiation treatment, or both, and these therapies are usually reserved for patients with metastatic or advanced disease [8]. The most appropriate therapy for metastasis to the breast is excisional biopsy, which should provide adequate local control [1,2,4,9]. Since mastectomy is not recommended unless the tumor is large or painful [4], accurate differentiation of the lesion from primary carcinoma is crucial if such surgery is to be avoided and appropriate systemic treatment begun promptly. Clinicians should be aware that distinguishing metastatic breast disease from a primary lesion can be difficult both radiologically and pathologically, especially in a patient who, like ours, has no history of malignant disease.

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REFERENCES

1. Vergier B, Trojani M, De Mascarel I, et al.: Metastases to the breast: Differential diagnosis from primary breast carcinoma. J Surg Oncol 48:112–116, 1991.
2. Hadju SI, Urban JA: Cancers metastatic to the breast. Cancer 29:1691–1696, 1972.
3. Toombs BD, Kalisher L: Metastatic disease to the breast: Clinical, pathologic and radiographic features. Am J Roentgenol 129:673–676, 1977.
4. Chaignaud B, Hall TJ, Powers C, et al.: Diagnosis and natural history of extramammary tumors metastatic to the breast. J Am Coll Surg 179:49–53, 1994.
5. Paulus DD, Libshitz HI: Metastasis to the breast. Radiol Clin North Am 20:561–567, 1982.
6. McIntosh IH, Hooper AA, Millis RR, Greening WP: Metastatic carcinoma within the breast. Clin Oncol 2:393–401, 1976.
7. Auerbach HE, Brooks JJ: Alveolar soft part sarcoma: A clinicopathologic and immunohistochemical study. Cancer 60:66–73, 1987.
8. Lieberman PH, Brennan MF, Kimmel M, et al.: Alveolar soft-part sarcoma: A clinico-pathologic study of half a century. Cancer 63:1–16, 1989.
9. Amichetti M, Perani B, Boi S: Metastases to the breast from extramammary malignancies. Oncology 47:257–260, 1990.
10. McCrea ES, Johnston C, Haney PJ: Metastases to the breast. AJR 141:685–690, 1983.
11. Heller DS, Frydman CP, Gordon RE, et al.: An unusual organoid tumor: Alveolar soft part sarcoma or paraganglioma? Cancer 67: 1894–1899, 1991.
12. Jochimsen PR, Brown RC. Metastatic melanoma in the breast masquerading as fibroadenoma. JAMA 236:2779–2780, 1976.
13. Ordóñez NG, Hickey RC, Brooks TE: Alveolar soft part sarcoma: A cytologic and immunohistochemical study. Cancer 61:525–531, 1988.
14. Bohman LG, Bassett LW, Gold RH, Voet R: Breast metastases from extramammary malignancies. Radiology 144:309–312, 1982.